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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,332	08/27/2003	Giulia Kennedy	3578.1	6861

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EXAMINER	
MYERS, CARLA J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,332	KENNEDY, GIULIA	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by Yu et al (U.S. Patent Application No. 20010036632) .

Yu (see, e.g., paragraph 101) teaches kits for detecting nucleic acid sequences. In particular, the kits of Yu contain all of the reagents required to detect a nucleic acid sequence, including (i) reagents for isolating and amplifying nucleic acids (i.e., reagents for obtaining a prenatal nucleic acid sample), (ii) a solid support (i.e., the solid support can be used for the purpose of genotyping at least 5000 SNPs) and (iii) labeling materials and means for assaying for a detectable label (i.e., reagents for analyzing genotypes to determine chromosomal abnormalities). Accordingly, the kits of Yu anticipate the claimed invention.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipshutz (US Application Publication No. 2002/0048749) in view of Bao (U.S. Patent No. 6,251,601).

Lipshutz teaches a method for diagnosing diseases and predisposition to diseases wherein the method comprises obtaining a nucleic acid sample, genotyping at least 10,000 SNPs in the nucleic acid sample, and analyzing the genotypes to identify chromosomal abnormalities (see, for example, paragraphs 22, 29 and 43). Lipshutz teaches that polymorphisms in a gene may be correlated with the occurrence of a mutation that alters protein function or alters replication, transcription or translation processes and that these chromosomal abnormalities can be correlated with a phenotype (paragraphs 63 and 64). Thereby, the polymorphic profile of an individual may be used to diagnose the likelihood that the individual will have or will develop a phenotypic trait associated with a chromosomal abnormality, such as one of the genetic diseases set forth in paragraph 64 of Lipshutz. Additionally, Lipshutz (paragraph 66) states that "(i)n the case of a strong correlation between a set of one or more polymorphic forms and a disease for which treatment is available, detection of the polymorphic form set in a human or animal may justify immediate administration of treatment, or at least the institution of regular monitoring of the patient. Detection of a polymorphic form(s) correlated with serious disease in a couple contemplating a family may also be valuable to the couple in their reproductive decisions. For example, the female partner might elect to undergo in vitro fertilization to avoid the possibility of transmitting such a polymorphism from her husband to her offspring." Accordingly,

Lipshutz teaches methods for diagnosing a disease by genotyping at least 10,000 SNPs but does not teach applying the diagnostic method to fetal nucleic acids for the purposes of prenatal diagnosis.

However, Bao (col. 18-24) teaches methods of prenatal diagnosis wherein the methods comprise obtaining a prenatal nucleic acid sample, genotyping the nucleic acid sample for chromosomal abnormalities and analyzing the chromosomal abnormalities to thereby provide a prenatal diagnosis. Bao teaches "prenatal arrays" that contain probes for detecting chromosomal abnormalities and mutations in oncogenes. Bao (col. 18) states that "(t)he human prenatal array is also useful for post-natal testing, for fetal cell testing and for pre-implantation genetic testing on blastomeres and polar bodies. "

In view of the teachings of Bao, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Lipshutz of simultaneously assaying for 10,000 or more SNPs to the analysis of fetal nucleic acids in order to have provided an accurate, efficient and effective means for prenatal diagnosis, thereby allowing for early intervention and genetic counseling in cases in which the fetus was determined to be susceptible to a genetic disease.

With respect to claim 2, Lipshutz does not teach analyzing a sample obtained by amniocentesis. However, Bao (col. 11, lines 56-66) teaches that fetal cells may be obtained from amniotic fluid and used for prenatal testing. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Lipshutz so as to have used fetal cells obtained by

amniocentesis because this would have provided a suitable and accessible source of fetal cells for prenatal diagnosis.

With respect to claims 5 and 6, Lipshutz teaches that the probes for detecting SNPs are present on a microarray (see, e.g., paragraph 52).

With respect to claim 11, Lipshutz teaches amplifying the sample nucleic acids prior to genotyping (see, e.g., paragraphs 33 and 37).

With respect to claims 7-10, Lipshutz (paragraph 33) teaches analyzing genomic DNA, but does snot teach the specific quantity of genomic DNA to be genotyped (i.e., a quantity of at least 250, 200, 150 or 100ng). However, Lipshutz does teach amplifying sample genomic nucleic acids prior to genotyping to obtain sufficient quantities of nucleic acids to ensure accurate detection of polymorphisms. Additionally, Bao (col. 11-12) teaches the need to use suitable quantities of nucleic acids for microarray analysis and teaches amplifying nucleic acids obtained from fetal cells in those cases in which only a few fetal cells are available. Bao (col. 13) teaches using sample nucleic acids in the range of 100 ng to 1 ug, and preferably 300 ng to about 425 ng for genetic analysis. To have determined the optimum quantity of nucleic acid to be genotyped would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,

456, 105 USPQ 233, 235 (CCPA 1955)." Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the optimal quantity of sample nucleic acids for genotyping, including quantities of at least 150-250 ng, since Bao teaches that these quantities are effective for microarray analysis and use of the optimal quantities of nucleic acids would have provided the most effective and accurate means of prenatal diagnosis.

3. Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipshutz in view of Bao and further in view of Kornman (U.S. Patent No. 6,733,967).

The teachings of Lipshutz and Bao are presented above. In particular, Bao teaches analyzing fetal cells obtained from amniotic fluid. However, neither Lipshutz nor Bao teach analyzing fetal cells obtained from chorionic villus samples or from fetal umbilical cord blood.

Kornman (col. 5-6 and 19-20) teaches methods of prenatal testing wherein samples of fetal nucleic acids are analyzed for the presence of a polymorphism. In particular, Kornman (col. 19-20) teaches that fetal cells may be obtained from chorionic villus sampling and from umbilical cord blood, as well as from amniocentesis samples.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Lipshutz and Bao so as to have used chorionic villus or umbilical cord blood samples in place of amniocentesis samples because these would have provided equally suitable sources of fetal cells for prenatal diagnosis.

4. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lipshutz in view of Bao and further in view of Ahern, H. (The Scientist. July 1995. Vol. 9, No. 155, pages 20-24).

The teachings of Lipshutz and Bao are presented above. In combination, the method of Lipshutz and Bao require the use of (i) reagents for obtaining a prenatal nucleic acid sample (e.g., reagents for isolating genomic DNA, or reagents for obtaining amniotic fluid samples), (ii) reagents for genotyping at least 5000 SNPs (e.g., an array for genotyping 10,000 SNPs, or a polymerase of amplifying target nucleic acids, or a solid support for immobilizing probes), and (iii) reagents for analyzing the genotypes (e.g., labels for detecting probe hybridization). Lipshutz and Bao do not teach packaging these reagents into a kit.

However, reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. In particular, Ahern discloses the general concept of kits for performing detection methods and discloses that kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatibility of the reagents to be used in the assay. Ahern (page 22) teaches that kits also provide the benefits of cost-effectiveness and time efficiency. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents for isolating fetal nucleic acids, reagents for genotyping 5000 SNPs and reagents for analyzing genotypes in a kit for the expected benefits of convenience and

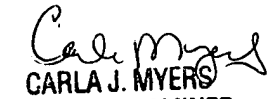
cost-effectiveness for practioners of the art wishing to practice the method prenatal diagnosis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
November 1, 2005



CARLA J. MYERS
PRIMARY EXAMINER